UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/011,940	03/03/1999	MICHAEL A. NAUCK	864861USWO	1535

7590 01/15/2002

FOLEY & LARDNER
3000 K STREET, N.W. STE.500
WASHINGTON, DC 20007-5109

EXAMINER	
CELSA, BENNETT M	

ART UNIT	PAPER NUMBER
1627	24

DATE MAILED: 01/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.	Applicant(s)
09/011,940	Nauck et al.
Examiner	**Art Unit**
Bennett Celsa	1627

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED *1/30/01 / 12/17/01* FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

a) ☒ The period for reply expires *three* months from the mailing date of the final rejection.

b) ☐ In view of the early submission of the proposed reply (within two months as set forth in MPEP § 706.07 (f)), the period for reply expires on the mailing date of this Advisory Action, OR continues to run from the mailing date of the final rejection, whichever is later. In no event, however, will the statutory period for the reply expire later than SIX MONTHS from the mailing date of the final rejection.

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will be entered upon the timely submission of a Notice of Appeal and Appeal Brief with requisite fees.

3. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search. (See NOTE below);

   (b) ☐ they raise the issue of new matter. (See NOTE below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

   NOTE: _____

4. ☒ Applicant's reply has overcome the following rejection(s):
   112 second paragraph rejection of claims 20, 41 and 44

5. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claim(s).

6. ☐ The a) ☐ affidavit, b) ☐ exhibit, or c) ☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because:

7. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

8. ☒ For purposes of Appeal, the status of the claim(s) is as follows (see attached written explanation, if any):

   Claim(s) allowed: _____

   Claim(s) objected to: _____

   Claim(s) rejected: *1, 2, 17-25, 32-35, and 41-50*

9. ☐ The proposed drawing correction filed on _____ a) ☐ has b) ☐ has not been approved by the Examiner.

10. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ .

11. ☒ Other: *See Attachment*

ADVISORY ACTION (CONT.)

Withdrawn Objection (s) and/or Rejection (s)

Applicant's amendment and argument has overcome the indefinite rejection of claims 20, 41 and 44.

Applicant's argument regarding the remaining rejections will be briefly addressed to the extent new issues are raised by applicant which were not previously addressed.

Outstanding Objection (s) and/or Rejection (s)

Claim Rejections - 35 USC § 112

1. Claim 21 (and claims dependent thereon) are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A. The new limitation of claim 21, e.g. "are administered at a rate of 0.01 ... per minute" constitutes new matter to extent that these recited amounts encompass parenteral administration means other than "infusion". In other words, the specification only provides support for this limitation with respect to administration by infusion.

Discussion

Applicant's amendment and arguments directed to the above new matter rejection were considered but deemed nonpersuasive for the following reasons.

Applicant argues that present claim 21 does not extend the scope of claim 21 as presented in the Preliminary Amendment.

Applicant's argument is not convincing since claim 21 is not an original claim and thus cannot provide original support for the presently claimed invention.

Accordingly, the specification range for infusion does not provide support for the same range as applicable to any means of administration

Accordingly, this rejection is hereby maintained

2. Claims 1-2, 17-19, 21-25, 32-35 and 41-48 are rejected under 35 U.S.C. 102(e) as being anticipated by Habener) as being anticipated by Habener, U.S. Pat. No 5,614,492 (3/97: filed 9/91 or earlier).

Habener "492 disclose the use of GLP 1 and its derivatives (e.g. col. 7) to treat both diabetes and hyperglycemia (e.g. see col. 6, lines 1-10) due to the peptide's "insulinotropic" activity (e.g. see col. 5, line 60-70). "Parenteral administration" of GLP 1 and its derivatives in pharmaceutical compositions comprising carbohydrates (e.g. lactose), polyamino acids: controlled release formulations comprising lipid derivatives (e.g. liposomes) e.g. see bottom of col. 9 to top of col. 10) as well as conjugates thereof (e.g. see col. 10, lines 13-26) anticipate the presently claimed invention. Further Example 11 (e.g. col. 21-28, especially "meal studies") disclose the administration of GLP-1 both during a meal (e..g 50% CHO; 30% fat; 20% protein: see e.g. col. 22, lines 55-67) and postprandial to both NORMAL and non-diabetic patients with the successful

control of plasma glucose levels. See also patent claims 1 and 9 (and dependent claims thereon) teaching the use of GLP-1 and derivatives to treat diabetes and hyperglycemia.

Accordingly, the parenteral administration of GLP-1 and its derivatives before/during/after meals that both contained and generated CHO (e.g. especially glucose) anticipates the presently claimed invention. See also patent claims which additionally disclose the treatment of both diabetes and hyperglycemia utilizing GLP-1 containing compositions.

Discussion

Applicant's arguments directed to the above anticipation rejection were considered but deemed nonpersuasive for the following reasons.

Applicant argues that this rejection to be sustainable must be interpreted to encompass the incorporation of trace materials. The Examiner respectfully disagrees.

The reference clearly incorporates the addition of compounds that are within the scope of the term "nutrients" (e.g. lactose, amino acids) both as separate compounds or as conjugates (e.g. see col. 9-10). Additionally, the patent reference further teaches administration of GLP compounds with a meal which presumably would contain nutrients (e.g. see col. 9-10 and examples).

Accordingly, the above rejection is hereby maintained.

3. Claims 1-2, 17-25, 32-35 and 41-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Specification disclosure as to the state of the prior art in view of Habener, U.S. Pat. No. 5,614,492 (3/97: filed 9/91 or earlier) and/or Eng US Pat. No. 5,424,286 (6/95) .

The specification on pages 1-2 and page 10, lines 15 describes the state of the prior art regarding the necessity for providing parenteral nutrition to patients having "disturbed glucose metabolism" (e.g. surgery patients, shock etc) as well as to malnourished patients while overcoming the hyperglycemia that accompanies parenteral nutrition. Coadministration of insulin with parenteral nutrition in order to overcome the hyperglycemia problem has its drawbacks (e.g. see page 1, lines 13-25).

The State of the Prior Art as described in the specification differs from the presently claimed invention which incorporates the use of "insulinotropic peptides" (e.g. GLP-1 and its derivatives) in parenteral nutrition compositions which comprise nutrients (e.g. glucose or glucose generating compounds) for alimentary nutrition or to treat hyperglycemic states.

However, both the Habener and Eng Patent references teach the "insulinotropic" nature of GLP-1 and related peptides e.g. the ability of these peptides to endogenously generate insulin and thus combat hyperglycemia.

Additionally, the prior/sequential and co-administration of these "insulinotropic" peptides with a meal containing nutrients (e.g. which include glucose or generate glucose) and the peptides concomitant ability to obtain normalized glucose levels is both disclosed and suggested by the Habener and/or Eng patents (e.g. see Habener, Example 11, col. 21-28 and patent claims

addressing treatment of diabetes and hyperglycemia; e.g. see Eng at col. 1, lines 49-67 disclosing lowering of meal-related glucose levels by parenteral administration of GLP-1 and GLIP which effect was also found with other "insulinotropic" peptides (e.g. exendins) alone or in combination (including sequential) with GLP-1 (e.g. see Eng col. 2, lines 35-40; col. 5, lines 14-20; Example 2 (col. 6-7); Example 5 relating to diabetics; and patent claims 5-6.

The determination of optimal amounts of "insulinotropic" peptides and/or nutrients taken sequentially or in combination is well within the skill of the art as well as the determination of optimal delivery formulations (e.g. tablets, pills, delayed release etc.) and time of delivery (e.g. coadministered, sequential etc.).

One of ordinary skill in the art would be motivated to substitute the "insulinotropic" peptides disclosed by the Eng or Habener references for insulin in "parenteral" formulations as disclosed in the Specification, due to the problematic use of insulin as discussed in the specification and in view of the ability of "insulinotropic peptides" to endogenously produce insulin as taught by the Eng and/or Habener references.

Accordingly, the incorporation of "insulinotropic" peptides (e.g. GLP-1 or its derivatives) into parenteral formulations containing "nutrients" to treat diabetics, non-diabetics (e.g. hyperglycemia) or malnourished individuals would have been obvious to one of ordinary skill in the art at the time of applicant's invention in view of the Habener and/or Eng references which demonstrate that administration of these peptides to obtain normalized glucose levels; regardless of the cause of hyperglycemia (meal/diabetes/hyperglycemia etc.).

Discussion

Applicant's arguments directed to the above obviousness rejection were considered but deemed nonpersuasive for the following reasons.

Applicant argues that Eng teaches removing "nutrients" (citing col. 4, lines 57-65).

Applicant's argument is misguided since Eng explicitly teaches compositions which are preferably free (e.g. "substantially free") of "natural contaminants". Accordingly, the Eng reference can not be interpreted as a teaching away of including nutrients but only a teaching toward removing impurities. In any event the Eng reference is not being cited for anticipation but for obviousness; and its teaching of the use of exendens for treating diabetes and preventing hypergylcemia presumably resulting from the insulinotropic acitivities of exendens is what is at issue in the above rejection.

As already discussed above and in arguments of record, applicant's teaching away argument regarding the Eng and/or Habener are untenable.

Applicant argues that substituting insulin with *insulinotropic* compounds (e.g. the Eng exendens or the Habener GLP compounds) would not have been obvious in light of the newly cited 1997 Nauck article.

In this respect applicant first asserts that the 1997 article "was generally available to one of ordinary skill in the art at the time of the invention".

The Examiner questions applicant's statement in two respects.

First, the Examiner is confused as to how a 1997 article would be available "at the time of the invention" (presumably applicant's invention) since applicant is claiming 119 priority to 1995? Or stated differently, the Examiner questions the relevancy of an article that was presumably published AFTER applicant's invention (presumably, unless applicant is not entitled to priority) to issues relating to anticipation or obviousness.

In any event applicant argues that the Nauck article demonstrates that GLP-1 (under the circumstances of the reference experiment) reduced insulin release (when administered non-parenterally) and did not stimulate insulin release as expected. Applicant apparently argues that this teaches away from GLP or other similar compound being insulinotropic.

Even assuming arguendo, that applicant's logic is correct, applicant's argument is misguided in a key respect. It would nevertheless be obvious to substitute one "hypoglcyemic agent" for another regardless of the presumed mechanism that causes the hypoglycemia. As discussed in the above rejection, hyperglycemia is the problem. If utilizing insulin for its hypoglycemia effects (REGARDLESS OF PRESUMED MECHANISM) has drawbacks why not substitute a different hypoglycemic agent??

Accordingly, the above obviousness rejection is hereby maintained.

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat (art unit 1627), can be reached at (703)308-0570.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa (art unit 1627)

January 11, 2002

BENNETT CELSA
PRIMARY EXAMINER